

FILE 'HOME' ENTERED AT 12:42:46 ON 05 NOV 2008

=> index bioscience

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 0.21 | 0.21 |

FULL ESTIMATED COST

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 12:43:14 ON 05 NOV 2008

69 FILES IN THE FILE LIST IN STINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (cholesterol (s) (ldl or (low (2a) density)) (s) total

UNMATCHED LEFT PARENTHESIS '(CHOLESTERO'

The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ((cholesterol (s) (ldl or (low (2a) density)) (s) total

UNMATCHED LEFT PARENTHESIS '((CHOLESTERO'

The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s cholesterol (s) (ldl or (low (2a) density)) (s) total

| | |
|----------------------|------------------|
| 4713 | FILE ADISCTI |
| 167 | FILE ADISINSIGHT |
| 711 | FILE ADISNEWS |
| 1771 | FILE AGRICOLA |
| 75 | FILE ANABSTR |
| 21 | FILE ANTE |
| 1 | FILE AQUALINE |
| 57 | FILE AQUASCI |
| 138 | FILE BIOENG |
| 11134 | FILE BIOSIS |
| 96 | FILE BIOTECHABS |
| 96 | FILE BIOTECHDS |
| 1082 | FILE BIOTECHNO |
| 6757 | FILE CABA |
| 8452 | FILE CAPLUS |
| 6 | FILE CEABA-VTB |
| 54 | FILE CIN |
| 10 | FILE CONFSCI |
| 4 | FILE CROPU |
| 30 | FILE DDFB |
| 3747 | FILE DDFU |
| 3672 | FILE DGENE |
| 568 | FILE DISSABS |
| 30 | FILE DRUGB |
| 7904 | FILE DRUGU |
| 27 FILES SEARCHED... | |
| 211 | FILE EMBAL |
| 13298 | FILE EMBASE |
| 6810 | FILE ESBIODASE |
| 1236 | FILE FROSTI |
| 1149 | FILE FSTA |
| 64 | FILE HEALSAFE |

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471 FILE IFIPAT
83 FILE IMSDRUGNEWS
251 FILE IMSPRODUCT
83 FILE IMSRESEARCH
6 FILE KOSMET
704 FILE LIFESCI
13657 FILE MEDLINE
27 FILE NTIS
71 FILE NUTRACEUT
7 FILE OCEAN
7776 FILE PASCAL
71 FILE PHAR
49 FILES SEARCHED...
92 FILE PHARMAML
1 FILE PHIC
228 FILE PHIN
1330 FILE PROMT
217 FILE PROUSDDR
10484 FILE SCISEARCH
5087 FILE TOXCENTER
94 FILE USGENE
3960 FILE USPATFULL
1 FILE USPATOLD
600 FILE USPAT2
15 FILE VETU
4 FILE WATER
626 FILE WPIDS
7 FILE WPIFV
626 FILE WPINDEX

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59 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L1 QUE CHOLESTEROL (S) (LDL OR (LOW (2A) DENSITY)) (S) TOTAL

=> s L1 (s) (esterase or lipase or dehydrogenase)

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24 FILE ADISCTI
4 FILE ADISINSIGHT
15 FILE ADISNEWS
47 FILE AGRICOLA
9 FILE ANABSTR
2 FILE AQUASCI
7 FILE BIOENG
57 FILE BIOSIS
10 FILE BIOTECHABS
10 FILE BIOTECHDS
72 FILE BIOTECHNO
235 FILE CABA
59 FILE CAPLUS
70 FILE DDFU
165 FILE DGENE
15 FILE DISSABS
171 FILE DRUGU
27 FILES SEARCHED...
2 FILE EMBAL
49 FILE EMBASE
257 FILE ESBIODASE
15 FILE FROSTI
37 FILE FSTA
3 FILE HEALSAFE
25 FILE IFIPAT
2 FILE IMSDRUGNEWS

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      4   FILE IMSRESEARCH
      1   FILE KOSMET
     41   FILE LIFESCI
     57   FILE MEDLINE
      1   FILE NTIS
    223   FILE PASCAL
50 FILES SEARCHED...
      1   FILE PHIN
      8   FILE PROMT
     52   FILE SCISEARCH
     25   FILE TOXCENTER
    282   FILE USPATFULL
     29   FILE USPAT2
     30   FILE WPIDS
     30   FILE WPINDEX

```

39 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L2 QUE L1 (S) (ESTERASE OR LIPASE OR DEHYDROGENASE)

=> s L2 (s) (surfactant or detergent or polyalkylene or polyoxyethylene)

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      1   FILE ANABSTR
      2   FILE BIOTECHABS
      2   FILE BIOTECHDS
      3   FILE CABA

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22 FILES SEARCHED...
      1   FILE DISSABS
      1   FILE ESBIOBASE
      5   FILE IFIPAT
      1   FILE LIFESCI

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44 FILES SEARCHED...
     14   FILE USPATFULL
      1   FILE USPAT2
      2   FILE WPIDS

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67 FILES SEARCHED...
      2   FILE WPINDEX

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12 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STINDEX

L3 QUE L2 (S) (SURFACTANT OR DETERGENT OR POLYALKYLENE OR POLYOXYETHYLENE)

=> d rank

```

F1      14   USPATFULL
F2       5   IFIPAT
F3       3   CABA
F4       2   BIOTECHABS
F5       2   BIOTECHDS
F6       2   WPIDS
F7       2   WPINDEX
F8       1   ANABSTR
F9       1   DISSABS
F10      1   ESBIOBASE
F11      1   LIFESCI
F12      1   USPAT2

```

=> fil f2-f12

COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 7.80 | 8.01 |

FILE 'IFIPAT' ENTERED AT 12:50:15 ON 05 NOV 2008
COPYRIGHT (C) 2008 IFI CLAIMS(R) Patent Services (IFI)

FILE 'CABA' ENTERED AT 12:50:15 ON 05 NOV 2008
COPYRIGHT (C) 2008 CAB INTERNATIONAL (CABI)

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'BIOTECHDS' ENTERED AT 12:50:15 ON 05 NOV 2008
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FILE 'WPIDS' ENTERED AT 12:50:15 ON 05 NOV 2008
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FILE 'WPINDEX' ACCESS NOT AUTHORIZED

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FILE 'LIFESCI' ENTERED AT 12:50:15 ON 05 NOV 2008
COPYRIGHT (C) 2008 Cambridge Scientific Abstracts (CSA)

FILE 'USPAT2' ENTERED AT 12:50:15 ON 05 NOV 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> s L3

L4 17 L3

=> dup rem L4

PROCESSING COMPLETED FOR L4

L5 14 DUP REM L4 (3 DUPLICATES REMOVED)

=> s L5 and py<2005

7 FILES SEARCHED...

L6 8 L5 AND PY<2005

=> d L6 ibib abs 1-8

L6 ANSWER 1 OF 8 IFIPAT COPYRIGHT 2008 IFI on STN
AN 10560327 IFIPAT;IFIUDB;IFICDB <<LOGINID::20081105>>

TITLE: Reagent for assaying lipid; Containing an
esterase; particularly to reagents for
assaying neutral fats, total
cholesterols, high-density lipoprotein
cholesterols, and/or low-
density lipoprotein cholesterol
for use in clinical chemistry; oxidation resistant
surfactant

INVENTOR(S): Shirahase; Yasushi, Kobe-shi, JP
Yamashita; Kazuaki, Kobe-shi, JP

PATENT ASSIGNEE(S): SYSMEX CORPORATION

AGENT: SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W.,
SUITE 800, WASHINGTON, DC, 20037, US

| | NUMBER | PK | DATE |
|--------------------------|----------------|----|----------|
| PATENT INFORMATION: | US 20040067545 | A1 | 20040408 |
| APPLICATION INFORMATION: | US 2003-633518 | | 20030805 |

| | NUMBER | DATE |
|------------------------|--|----------|
| PRIORITY APPLN. INFO.: | JP 2002-232695 | 20020809 |
| FAMILY INFORMATION: | US 20040067545 | 20040408 |
| | US 7074581 | 20060711 |
| DOCUMENT TYPE: | Utility | |
| | Patent Application - First Publication | |
| FILE SEGMENT: | CHEMICAL | |
| | APPLICATION | |
| ENTRY DATE: | Entered STN: 11 Apr 2004 | |
| | Last Updated on STN: 6 Oct 2005 | |

NUMBER OF CLAIMS: 20

AB Effective stabilizing amount at least of one antioxidant is added to a composition containing an esterase and surfactant(s).

CLMN 20

L6 ANSWER 2 OF 8 CABA COPYRIGHT 2008 CABI on STN

ACCESSION NUMBER: 97:148220 CABA <<LOGINID::20081105>>

DOCUMENT NUMBER: 19971411415

TITLE: Clinical efficacy of the direct assay method using polymers for serum high density lipoprotein cholesterol

AUTHOR: Shirai, K.; Nema, T.; Hiroh, Y.; Itoh, Y.; Miyashita, Y.; Watanabe, H.

CORPORATE SOURCE: Clinical Laboratory Medicine, Sakura Hospital, Toho University School of Medicine, Sakura 285, Japan.

SOURCE: Journal of Clinical Laboratory Analysis, (1997) Vol. 11, No. 2, pp. 82-86. 9 ref. ISSN: 0887-8013

DOCUMENT TYPE: Journal

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Dec 1997

Last Updated on STN: 11 Dec 1997

AB LDL and VLDL were coated with polymers and polyanions to block cholesterol esterase and cholesterol oxidase. The reduction of these enzymes for HDL cholesterol was enhanced with a detergent, and HDL cholesterol was selectively measured. Within-run (n=3, 20 times) and between-run (n=3, 7 days) CVs were <2%. The repeated freezing and thawing (4 times) of 3 distinct sera resulted in no changes in HDL cholesterol values. Additions of lipid emulsion (triglyceride 100 mg/100 ml) and free bilirubin (20 mg/100 ml) had no effect. Linearity was found up to 300 mg/100 ml. Increases in HDL cholesterol values by the addition of VLDL (total cholesterol (TC) 300 mg/100 ml) or LDL (TC 300 mg/100 ml) to the tested sera were <0.5%. The correlation coefficient of the new method with a precipitation method was 0.995 (n=64). HDL-C values for patients with hyperlipaemia (Type IIa, IIb, or III, IV, and V) by this method were comparable with those obtained by the precipitation method. It is concluded that the new method meets the requirements for accuracy, precision and ease of handling numerous samples.

L6 ANSWER 3 OF 8 CABA COPYRIGHT 2008 CABI on STN

ACCESSION NUMBER: 82:79189 CABA <<LOGINID::20081105>>

DOCUMENT NUMBER: 19811428713

TITLE: Hyperlipidemia in rats fed retinoic acid

AUTHOR: Gerber, L. E.; Erdman, J. W., Jr.
CORPORATE SOURCE: Dep. Food Science, Univ. Illinois, Urbana, IL 61801, USA.
SOURCE: Lipids, (1981) Vol. 16, No. 7, pp. 496-501. 29 ref.
ISSN: 0024-4201
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Nov 1994
Last Updated on STN: 1 Nov 1994

AB After young adult male Sprague-Dawley rats had been given 1.2 retinol equivalents retinyl acetate plus supplemental retinoic acid (100 mu g/g dry diet) for 3 days and deprivation of food for 6 to 8 h, triglyceride, cholesterol and phospholipid were estimated in serum lipoprotein fractions. Compared with controls, the serum very-low-density lipoprotein (VLDL) and the high-density lipoprotein (HDL) fractions of rats given retinoic acid had an increased triglyceride content. Whereas VLDL cholesterol and phospholipids were also increased, total serum cholesterol and phospholipids were not changed. The detergent Triton WR-1339 was used to depress serum triglyceride clearance to assess the effects of retinoic acid feeding on serum triglycerides. Triglyceride accumulation started earlier after Triton treatment and was greater when rats were given retinoic acid 100 mu g/g for 3 days before testing. Red and white gastrocnemius muscle, cardiac ventricular muscle and perirenal adipose tissue were removed from rats after retinoic acid feeding. Lipoprotein lipase (EC 3.1.1.3) activity showed a decrease in adipose tissue, a large depression in both areas of gastrocnemius muscle and no change in cardiac muscle as a result of retinoic acid feeding.

L6 ANSWER 4 OF 8 BIOTECHDS COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2000-08277 BIOTECHDS <LOGINID:20081105>
TITLE: Methods for fractional quantification of cholesterol in lipoproteins in biological samples such as serum which is applicable by simple automatic procedure, useful for clinical diagnosis;
cholesterol quantification method in low density and high density lipoprotein using cholesterol-esterase, cholesterol-oxidase and cholesterol-dehydrogenase for diagnosis

AUTHOR: Sugiuchi H
PATENT ASSIGNEE: Kyowa-Medex
LOCATION: Tokyo, Japan.
PATENT INFO: WO 2000017388 30 Mar 2000
APPLICATION INFO: WO 1999-P 47128 30 Jul 1999
PRIORITY INFO: JP 1998-264367 18 Sep 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-283609 [24]

AN 2000-08277 BIOTECHDS <LOGINID:20081105>

AB A method for quantifying low density and/or high density lipoproteins (LDL and HDL, respectively) cholesterol in a biological sample, which involves obtaining a sample, mixing it with cholesterol-esterase (EC-3.1.1.13), cholesterol-oxidase (EC-1.1.3.6) or cholesterol-dehydrogenase and then reaction the cholesterol with its specific cholesterol enzyme in the presence of a reagent for generating hydrogen peroxide or reduced co-enzyme, is new. Also claimed are: a method for fractional quantification of HDL cholesterol and total cholesterol in a biological sample; a reagent for the reaction of

cholesterol in all lipoproteins which contains a surfactant that can dissolve the lipoprotein; a quantification reagent for LDL cholesterol which consists of a cholesterol enzyme and a reagent to act on the LDL cholesterol-specific cholesterol enzyme; a reagent kit for the fractional quantification of HDL and LDL cholesterol; and a reagent kit for the fractional quantification of HDL and total cholesterol. The above may be useful for the clinical diagnosis of diseases related to high cholesterol levels in lipoproteins, such as arteriosclerosis. (46pp)

L6 ANSWER 5 OF 8 BIOTECHDS COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 1988-07462 BIOTECHDS <<LOGINID::20081105>>
TITLE: Specific measurement of high density lipoprotein cholesterol in serum;
using cholesterol-esterase and cholesterol-oxidase
PATENT ASSIGNEE: Boehr.Mannheim
PATENT INFO: EP 265933 4 May 1988
APPLICATION INFO: EP 1987-115841 28 Oct 1987
PRIORITY INFO: DE 1986-636851 29 Oct 1986
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 1988-121051 [18]
AN 1988-07462 BIOTECHDS <<LOGINID::20081105>>
AB Specific determination of high density lipoprotein (HDL) cholesterol in the presence of the low density lipoprotein-fraction of serum lipoproteins comprises treatment with cholesterol-esterase (CE, EC-3.1.1.13) to release cholesterol, which is oxidized with cholesterol-oxidase (CO, EC-1.1.3.6) and O₂ to form H₂O₂, the kinetics of formation being measured. The measurement is taken 2-15 min after the start of the oxidation reaction at 20-40 deg, especially 25-37 deg, for a predetermined time interval. During measurement the concentrations of CE, CO, bile acid surfactant and nonionic surfactant are kept at 0.05-30 u/ml, 0.1-50 u/ml, 1-20 mM (especially 1.5-8 mM) and 0.1-10 g/l (especially 0.4-4.0 g/l), respectively and the pH is 5-9. The reagent which supplies the specified concentrations of components, the pH 5-9 buffer and the H₂O₂ measuring system are new. The HDL component is measured with a simple reagent in a single step and the sample can also be used for measurement of total cholesterol. The nonionic detergent, especially a polyethyleneoxy compound, is added 1-14 min before measurement, especially 3-10 min after the start of oxidation. (16pp)

L6 ANSWER 6 OF 8 WPIDS COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2004-525059 [50] WPIDS
DOC. NO. CPI: C2004-193203 [50]
DOC. NO. NON-CPI: N2004-416125 [50]
TITLE: Simultaneous measurement of cholesterol in low-density lipoprotein, and total cholesterol in a biological sample, comprises quantifying cholesterol and total cholesterol in a single measurement procedure
DERWENT CLASS: B04; D16; S03
INVENTOR: MATSUI H
PATENT ASSIGNEE: (DENK-N) DENKA SEIKEN KK; (MATS-I) MATSUI H
COUNTRY COUNT: 106

PATENT INFO ABBR.:

| PATENT NO | KIND DATE | WEEK | LA | PG | MAIN IPC |
|-----------|-----------|------|----|----|----------|
|-----------|-----------|------|----|----|----------|

| | | | | | | |
|----------------|----|----------|------------|----|-------|-----|
| WO 2004055204 | A1 | 20040701 | (200450) * | JA | 28[3] | <-- |
| AU 2003289081 | A1 | 20040709 | (200474) | EN | | <-- |
| EP 1577398 | A1 | 20050921 | (200562) | EN | | <-- |
| US 20060078958 | A1 | 20060413 | (200626) | EN | | |
| JP 2004560637 | X | 20060420 | (200628) | JA | 19 | |
| KR 2005085539 | A | 20050829 | (200644) | KO | | |
| CN 1748036 | A | 20060315 | (200649) | ZH | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|----------------|------|------------------|----------|
| WO 2004055204 | A1 | WO 2003-JP15995 | 20031212 |
| AU 2003289081 | A1 | AU 2003-289081 | 20031212 |
| EP 1577398 | A1 | EP 2003-778913 | 20031212 |
| EP 1577398 | A1 | WO 2003-JP15995 | 20031212 |
| US 20060078958 | A1 | WO 2003-JP15995 | 20031212 |
| JP 2004560637 | X | WO 2003-JP15995 | 20031212 |
| KR 2005085539 | A | WO 2003-JP15995 | 20031212 |
| JP 2004560637 | X | JP 2004-560637 | 20031212 |
| US 20060078958 | A1 | US 2005-537992 | 20050609 |
| KR 2005085539 | A | KR 2005-710592 | 20050610 |
| CN 1748036 | A | CN 2003-80109741 | 20031212 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|-----------------|
| AU 2003289081 | A1 Based on | WO 2004055204 A |
| EP 1577398 | A1 Based on | WO 2004055204 A |
| JP 2004560637 | X Based on | WO 2004055204 A |
| KR 2005085539 | A Based on | WO 2004055204 A |

PRIORITY APPLN. INFO: JP 2002-362970 20021213

AN 2004-525059 [50] WPIDS

AB WO 2004055204 A1 UPAB: 20060121

NOVELTY - Simultaneous measurement (M1) of cholesterol in low-density lipoprotein, and total cholesterol in a biological sample, comprises quantifying cholesterol and total cholesterol in a single measurement procedure.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a reagent composition (I) for carrying out (M1).

USE - (M1) is useful for simultaneous measurement (M1) of cholesterol in low-density lipoprotein, and total cholesterol in a biological sample (claimed).

ADVANTAGE - (M1) enables a simultaneous measurement of cholesterol in low-density lipoprotein, and total cholesterol in a biological sample (claimed).

L6 ANSWER 7 OF 8 ANABSTR COPYRIGHT 2008 RSC on STN

AB The analytical and clinical performance of two low-density lipoprotein cholesterol (LDL-C) assays (LDL-CRD, Roche Diagnostics and LDL-CGZ, Genzyme) were evaluated simultaneously as well as those calculated by the Friedewald calculation (LDL-CFried) (cf., Friedewald et al.), Clin. Chemical, 1972, 18, 499). LDL-CRD utilizes the fact that at a neutral pH value (7.0) in the presence of MgCl2, sulfated α -cyclodextrin and dextran sulfate, the enzymatic reaction for cholesterol in very low-density lipoprotein

(VLDL) is markedly reduced (reagent 1). The non ionic detergent in reagent 2, selectively solubilizes LDL-C, enables measured of LDL-C by a conventional enzymatic reaction (cf., Suguchi et al., Clin. Chemical, 1998, 44, 522). The assay was calibrated and performed according to the manufacturer's recommendation. In the LDL-CGZ method (Genzyme, Cambridge, MA, USA), reagent 1 contains a detergent which solubilizes all non-LDL lipoproteins. The enzymes cholesterol esterase and cholesterol oxidase react with the non-LDL cholesterol. In the second step another detergent solubilizes the LDL-C so that it can be easily measured with a conventional enzymatic reaction (cf., Rifai et al., Clin. Chemical, 1998, 44, 1242). As before, the assay was performed according to the manufacturer's recommendations. Results (tabulated) showed that in order to classify someone correctly into the recommended National Cholesterol Education Program cut points, the total error requirement ($\leq 12\%$), was met by the LDL-CGZ assay at all clinical decision cut-points, whereas the LDL-CND assay only met the requirement at concentrations of 4.92 mmol/l. The LDL-Cfried failed to meet the total error requirement, because the compounded imprecision of the three independent tests required for this calculation was high. At the medical decision cut-point range, LDL -CRD, LDL-CGZ and LDL-CFried assays showed positive predictive values of 89-100, 85-100 and 83-99%, respectively, and negative predictive values of 52-98, 77-98 and 68-98%, respectively.

L6 ANSWER 8 OF 8 DISSABS COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved on STN
 ACCESSION NUMBER: 1998:32674 DISSABS Order Number: AARMQ24831
 TITLE: ALTERED PLASMA MEMBRANE CHOLESTEROL IN NIEMANN-PICK TYPE II DISEASE
 AUTHOR: DEGANI, NIKHAT [M.SC.]; BYERS, DAVID M. [adviser]
 CORPORATE SOURCE: DALHOUSIE UNIVERSITY (CANADA) (0328)
 SOURCE: Masters Abstracts International, (1997) Vol. 36, No. 4, p. 1073. Order No.: AARMQ24831. 98 pages. ISBN: 0-612-24831-3.
 DOCUMENT TYPE: Dissertation
 FILE SEGMENT: MAI
 LANGUAGE: English
 AB

Niemann-Pick type II disease is an autosomal recessive, cholesterol storage disorder that leads to severe neurodegeneration and death usually by the second decade. The genetic defect inhibits processing of low density lipoprotein (LDL)-derived cholesterol resulting in lysosomal accumulation and impaired regulation of cholesterol synthesis, uptake, and esterification. The present study attempted to determine whether specific cholesterol domains within the plasma membrane might be affected in this disorder. Three separate approaches were taken: measurement of plasma membrane cholesterol efflux, plasma membrane sensitivity to permeabilization by the detergent digitonin, and analysis of caveolar domains. Efflux of plasma membrane ^3H -cholesterol under conditions of plasma membrane labelling (1h preincubation with label) was much more rapid to methyl- β -cyclodextrin ($t_{1/2} < 30$ min) than to either LDL or HDL ($t_{1/2} = 10$ - 15 h) and occurred at similar rates for both cell types. Basal efflux was also comparable in both normal and Niemann-Pick type II cells. Similar results were obtained when total cellular cholesterol was labelled (48 hour preincubation with label), indicating that regions of cholesterol participating in cholesterol efflux are not significantly altered in Niemann-Pick type II disease. Release of lactate

dehydrogenase, a cytosolic enzyme, was assayed as an indicator of susceptibility of cholesterol-rich domains of the plasma membrane to digitonin permeabilization. At low concentrations of digitonin ($0.5 \mu\text{g/ml}$), release of lactate dehydrogenase was increased in control relative to Niemann-Pick cells, indicating that Niemann-Pick fibroblasts may have deficiencies in certain cholesterol-rich domains of the plasma membrane. However, no cell-specific differences in caveolin levels, caveolin extraction, or phosphotyrosine levels within caveolar domains were observed, suggesting that these cholesterol-rich regions may be conserved in Niemann-Pick type II disease.

=> logoff